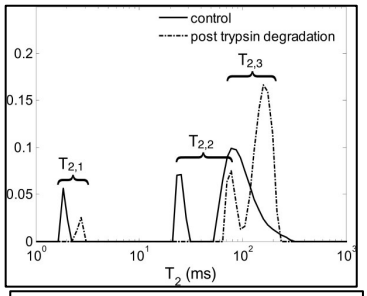
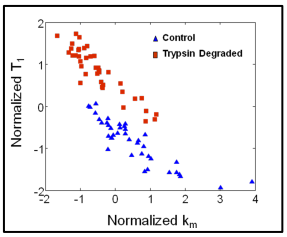
Magnetic Resonance Imaging and Spectroscopy Section (MRISS), Richard G. Spencer, M.D., Ph.D.

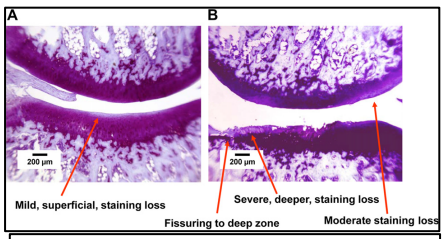
The activities of this Section center around the development of novel MR approaches to assess cartilage, with a specific emphasis on work with translational potential. The imaging and spectroscopy platforms used are preclinical 7T horizontal bore and 9.4T vertical bore MR systems, and the 3T human system at Harbor Hospital. Although, in some sense, MR studies of cartilage represent a mature field, the widely-used outcome measures provide only limited molecular-level information and are only moderately sensitive and specific to cartilage disease. We have therefore initiated two categories of non-conventional approaches to cartilage diagnosis. **First, we previously introduced multi-exponential transverse relaxation analysis to identify underlying macromolecular compartments in normal and degraded cartilage (figure to left). This has now been extended in several ways, based on much more general approaches to parameter estimation for the relaxation signal in MR.** These include i) multidimensional experiments, permitting a much more complete characterization of molecular compartments; ii) compressed sensing, rendering multidimensional experiments more realistic in terms of acquisition time; iii) incorporation of non-multiexponential signal models; iv) sample rotation experiments and exchange simulations to further illuminate the nature of multicomponent relaxation and intercompartment transport; and analyses centering around the ill-posed mathematical nature of parameter estimation from exponential decays, including v) demonstration of the importance of incorporating the Rician noise model into signal analysis for complex signals; and vi) rigorous bounds on parameter estimation in complex models and development of Bayesian methods as a method to improve these estimates, avoiding may of the problems of non-linear least squares analysis. We note that these highly inter-related studies, while in some cases mathematical in nature, are all supported by extensive experimental investigations and are all targeted to the very difficult problem of non-invasive macromolecular characterization of normative and degraded cartilage. **Second, we have introduced multivariate statistical methods into cartilage analysis with an emphasis on diagnostic performance (figure to right).** These have been extended to i) more advanced analyses, including the support vector machine and support vector regression to characterize biochemical and mechanical properties of cartilage; ii) incorporation of variables from multiexponential analysis into multivariate analyses; iii) translational approaches, using MR intensities routinely obtained in clinical research, including in the Osteoarthritis Initiative (OAI), and studies of human cartilage samples; iv) formal mathematical analyses of test characteristics based on MR outcome measures. Again, all of these approaches are firmly centered about the highly clinical goal of improving the ability of MR studies to diagnose osteoarthritis. **An additional significant development in the MRISS has been to initiate and to obtain funding, with collaborators, for a multi-site pilot clinical trial of pulsed low-intensity ultrasound (PLIUS) to treat OA.** This initiative is firmly grounded in a large number of pre-clinical studies of the effect of PLIUS on cartilage performed by many groups, including the MRISS (figure to left). If successful, this trial, funded through the Veterans Administration Cooperative Clinical Trials program, would strongly support a follow-up definitive trial of PLIUS for OA, which could lead to the first disease-modifying intervention for this age-associated disease with a profound morbidity burden. **Dr. Spencer also collaborates extensively with other intramural scientists who wish to incorporate body or brain imaging into their studies.** Finally**, Dr. Spencer serves as Director of the MRI Core Facility for Translational Research, with ongoing clinical research activities** in collaboration with clinical investigators, including those within the BLSA. This research program focuses on bioenergetic underpinnings of functional outcomes, muscle signal analysis to obtain correlates with age and sarcopenia, body composition analysis, and several human studies initiated by NIA collaborators.



Multiexponential analysis of bovine nasal cartilage, pre- and post-trypsin degradation.



Control and degraded BNC samples in feature space, illustrating the relationship between **k**m and **T**1.



Results for treatment of Guinea pig joints initiated at 2 months of age, with treatment duration 4 months. Left: PLIUS-treated. Right: Untreated control animal.